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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/546,000	06/14/2006	Hirofumi Hamada	50026/054001	8449

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EXAMINER	
HILL, KEVIN KAI	
ART UNIT	**PAPER NUMBER**
1633	

NOTIFICATION DATE	DELIVERY MODE
11/01/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentadministrator@clarkelbing.com

Office Action Summary	Application No.	Applicant(s)	
	10/546,000	HAMADA ET AL.	
	Examiner	Art Unit	
	Kevin K. Hill, Ph.D.	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 August 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) *1-13,15,18 and 19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14,16,17,20 and 21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

Applicant's responses to the Requirement for Restriction, filed on June 29, 2007 and August 31, 2007, is acknowledged.

Applicant has elected without traverse the invention of Group III, claim(s) 14-17, drawn to a therapeutic composition comprising a genetically modified mesenchymal cell comprising a foreign gene encoding angiopoietin-1.

Within Group III, Applicant has elected the minus-strand RNA viral vector species "i", as recited in Claim 16.

Amendments

In the reply filed June 29, 2007, Applicant has added new claims, claims 20-21. Applicant's new claims have been entered into the application as requested and will be examined on the merits herein, as they are considered to belong to the elected group.

Claims 1-13, 15 and 18-19 are pending but withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a non-elected invention, there being no allowable generic or linking claim.

Claims 14, 16-17 and 20-21 are under consideration.

Priority

This application is a 371 of PCT/JP04/00957, filed January 30, 2004. Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged

Acknowledgment is also made of Applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). The certified copy of JP 2003-040806, filed February 19, 2003 is filed with the instant application.

Accordingly, the effective priority date of the instant application is granted as February 19, 2003.

Information Disclosure Statement

Applicant has filed Information Disclosure Statements on September 15, 2005, July 7, 2006, August 22, 2006, June 11, 2007 and June 15, 2007.

The IDS filed September 15, 2005 is defective because Applicant has not provided copies of Hattori et al (2001), Schwarz et al (2000), and Takakura et al (2000). The listing of references in the Search Report is not considered to be an information disclosure statement (IDS) complying with 37 CFR 1.98. 37 CFR 1.98(a)(2) requires a legible copy of: (1) each foreign patent; (2) each publication or that portion which caused it to be listed; (3) for each cited pending U.S. application, the application specification including claims, and any drawing of the application, or that portion of the application which caused it to be listed including any claims directed to that portion, unless the cited pending U.S. application is stored in the Image File Wrapper (IFW) system; and (4) all other information, or that portion which caused it to be listed. In addition, each IDS must include a list of all patents, publications, applications, or other information submitted for consideration by the Office (see 37 CFR 1.98(a)(1) and (b)), and MPEP § 609.04(a), subsection I. states, "the list ... must be submitted on a separate paper." Therefore, the references cited in the Search Report have not been considered. Applicant is advised that the date of submission of any item of information or any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the IDS, including all "statement" requirements of 37 CFR 1.97(e). See MPEP § 609.05(a).

The citation of Takahashi et al (2003) in the IDS filed August 22, 2006 is lined through because it is a duplicate ("Dup.") of the citation in the IDS filed September 15, 2005.

The IDS filed June 15, 2007 is not considered because Applicant has not provided an English translation of CN 1353185 A, as indicated.

The Examiner has considered the remaining references in the Information Disclosure Statements, and signed/dated copies are mailed with this action.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

1. **Claims 14 and 16 are rejected under 35 U.S.C. 101** because the claimed invention is directed to non-statutory subject matter. In *Diamond v. Chakrabarty*, 447 U.S. 303, 206, USPQ 193 (1980), the Supreme Court set forth several tests for weighing whether patentable subject matter under 35 U.S.C. 101 is present, stating that:

"The relevant distinction was not between living and inanimate things but between products of nature, whether living or not, and human-made inventions. [A] new mineral discovered in the earth or a new plant found in the wild is not patentable subject matter."

In the instant case, the claims are drawn to a genetically modified mesenchymal cell comprising a foreign gene encoding angiopoietin-1. While the "hand of man" was required to obtain the polynucleotide sequence and deliver the foreign gene to the cell, the claims as written, do not sufficiently distinguish a cell as it exists naturally in the body of a [human] patient. The claims are directed to "host cells" transduced with a foreign gene, without restriction as to where the cell is located. The specification describes administering the genetically modified host cells to patients for treatment of diseases. It is implicit that such patients are mainly human. Consequently, when read in light of the specification the claimed host cells would include host cells in human patients that would be an integral and inseparable part of the human. Such cells that are part of a human are non-statutory subject matter since they embrace the human that carries them. It is USPTO policy not to allow claims to humans (1077 O.G. 24 April 1987). The claims should be amended to indicate the hand of the inventor, e.g., by insertion of "isolated " before cells. See MPEP 2105.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the Applicant regards as his invention.

2. **Claim 16 is rejected under 35 U.S.C. 112, second paragraph**, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. It is unclear if the claim is reciting a limitation of the vector encoding the foreign gene of claim 14, or if the genetically modified mesenchymal cell is transfected with a second vector encoding Ang-1, wherein the second vector is a minus-strand RNA viral vector, specifically a Sendai viral vector.

Clarification and/or correction is required.

To the extent that the specification discloses that the mesenchymal cell is transfected with only one vector encoding the foreign Ang-1 gene, in the interest of compact prosecution, the Examiner interprets the recitation of claim 16 to mean that the vector responsible for introducing the foreign Ang-1 gene is a minus-strand RNA viral vector.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the Applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the Applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the Applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the

international application designated the United States and was published under Article 21(2) of such treaty in the English language.

3. **Claim 14 is rejected under 35 U.S.C. 102(a)** as being anticipated by Nykanen et al, Circulation 107(9):1308-1314, 2003; available online February 17, 2003; *of record in IDS).

Nykanen et al teach cardiac mesenchyme infected with a foreign gene encoding Ang-1 (pg 1310, Figure 2).

4. **Claim 14 is rejected under 35 U.S.C. 102(b)** as being anticipated by Chae et al, Arterioscler. Thromb. Vasc. Biol. 20(12): 2573-2578, 2000; *of record in IDS).

Chae et al teach the intramuscular injection of plasmid encoding Ang-1 (pg 2574, col. 1, Gene Transfer). Chae et al teach that semi-membranous muscles were transfected with the foreign gene (pg 2576, col. 2, ¶1). To the extent that the specification broadly defines "mesenchymal cell" (pgs 17, lines 24-26; pg 22, lines 30-36), the capillary and semi-membranous muscle cells are reasonably interpreted as mesenchymal cells.

5. **Claims 14 and 17 are rejected under 35 U.S.C. 102(a) and 35 U.S.C. 102(e)** as being anticipated by Ueno et al (US 2002/0037278 A1).

Ueno et al disclose bone-marrow derived mononuclear cells transfected with a nucleic acid encoding Ang-1, wherein said transfected cells may be used in a method of delivering a recombinant nucleic acid molecule to a disease, damaged, ischemic or angiogenic site in a subject by transplantation at or near the site of disease in the context of a pharmaceutically acceptable carrier, e.g. saline (pg 1, [0008]; pg 5, [0042]; pg 8, [0074]).

Ueno et al disclose that the nucleic acid molecule encoding the foreign gene may be introduced into the host mesenchymal cell using any one of a genus of viral vectors known in the art (pg 6, [0048]).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the Examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the Examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. **Claims 14, 16-17 and 20-21 are rejected under 35 U.S.C. 103(a)** as being unpatentable over Ueno et al (US 2002/0037278 A1) and Sakai et al (FEBS Letters 456:221-226, 1999).

Ueno et al disclose bone-marrow derived mononuclear cells [mesenchymal cells] transfected with a nucleic acid encoding Ang-1, wherein said transfected cells may be used in a method of delivering a recombinant nucleic acid molecule to a disease, damaged, ischemic or angiogenic site in a subject by transplantation at or near the site of disease in the context of a pharmaceutically acceptable carrier, e.g. saline (pg 1, [0008]; pg 5, [0042]; pg 8, [0074]). Ueno et al disclose that the nucleic acid molecule encoding the foreign gene may be introduced into the host mesenchymal cell using any one of a genus of viral vectors known in the art (pg 6, [0048]).

Ueno et al do not disclose the use of a minus-strand RNA viral vector, specifically a Sendai viral vector to deliver the angiopoietin foreign gene to the cell. However, at the

time of the invention, Sakai et al taught the development of minus-strand RNA Sendai virus vectors to express foreign genes.

It would have been obvious to one of ordinary skill in the art to substitute the viral vector of Ueno et al with a minus-strand RNA Sendai virus vector as taught be Sakai et al with a reasonable chance of success because the simple substitution of one viral vector for another would have yielded predictable results to one of ordinary skill in the art at the time of the invention. Furthermore, a minus-strand RNA viral vector is not considered an essential feature of the invention in light of the disclosure that the foreign gene encoding Ang-1 may also be delivered via non-minus-strand RNA viral vectors, e.g. an adenoviral vector, an adeno-associated viral vector, a retroviral vector, a lentiviral vector, a herpes simplex virus vector, and a vaccinia virus vector (pg 12, lines 8-10). An artisan would be motivated to use a minus-strand RNA Sendai virus vector to express a foreign gene because Sakai et al teach that Sendai viruses reach a high copy number in infected cells, possesses a broad cellular host range, including non-dividing cells and peripheral mononuclear [mesenchymal] cells, achieve a high level of foreign gene expression, and is extremely useful in producing large quantities of medically important proteins in cells of interest (pg 224, Figure 3B, pg 226, col. 1, ¶2 and col. 2).

Thus, the invention as a whole is *prima facie* obvious.

Conclusion

7. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Kevin K. Hill, Ph.D. whose telephone number is 571-272-8036. The Examiner can normally be reached on Monday through Friday, between 9:00am-6:00pm EST.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Joseph T. Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Q. JANICE LI, M.D.
PRIMARY EXAMINER